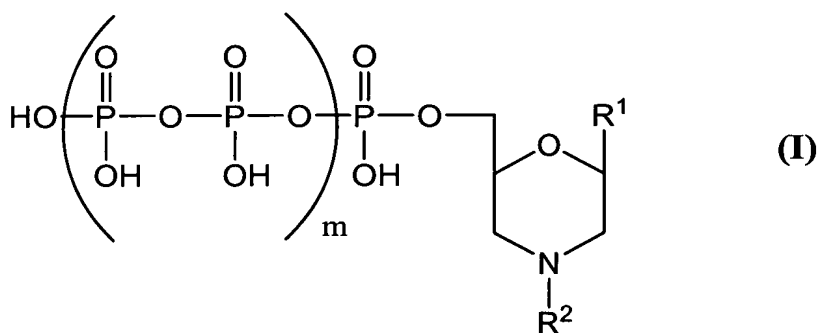


That which is claimed is:

1. Process for manufacturing a nucleic acid fragment comprising enzymatically incorporating at the 3' OH end of the nucleic acid fragment a modified morpholino-nucleotide having as precursor a compound of formula:



in which  $\text{R}^1$  represents a nucleic base,  $m$  is 0 or 1 and  $\text{R}^2$  is selected from the group consisting of:

- |                                   |                                 |
|-----------------------------------|---------------------------------|
| - $(\text{CH}_2)_n\text{-NH}_2$   | - $(\text{CH}_2)_n\text{-SH}$   |
| - $(\text{CH}_2)_n\text{-COOH}$   | - $(\text{CH}_2)_n\text{-OH}$   |
| - $(\text{CH}_2)_n\text{-NH-R}^3$ | - $(\text{CH}_2)_n\text{-SR}^3$ |
| - $(\text{CH}_2)_n\text{-CO-R}^3$ | - $(\text{CH}_2)_n\text{-OR}^3$ |
- and

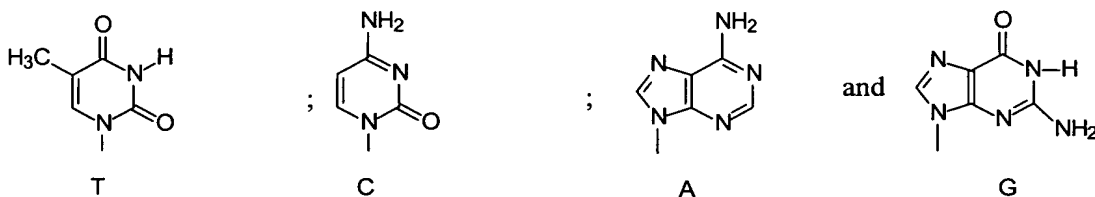
in which  $n$  is an integer ranging from 1 to 12 and  $\text{R}^3$  is selected from the group consisting of a label, a protein, an enzyme, a fatty acid, and a peptide.

2. Process according to Claim 1, in which an enzyme of said enzymatic incorporation is the Klenow fragment of DNA polymerase.

3. Process according to Claim 1, in which an enzyme of said enzymatic incorporation is selected from the group consisting of a heat-resistant polymerase of a *Thermophilus* bacterium, a terminal transferase, and reverse transcriptase.

4. Process according to Claim 1, in which the nucleic base is a natural nucleic base selected from the group consisting of adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine, and 2-aminopurine.

5. Process according to Claim 1, in which R<sup>1</sup> is selected from the group consisting of:



6. Process according to Claim 1, in which the label is selected from the group consisting of radioactive products, luminescent products, electroluminescent and fluorescent products, and enzymatic labels.

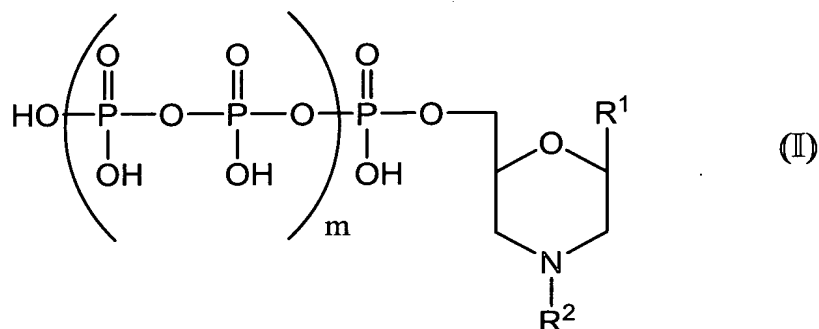
7. Process according to Claim 1, in which R<sup>3</sup> is a fluorophore.

8. Process according to Claim 1, in which R<sup>3</sup> is selected from the group consisting of fluorescein, biotin, and rhodamine.

9. Process according to Claim 1, in which the modified-morpholino nucleotide is compound (I) in which m is 0.

10. Process according to Claim 1, in which R<sup>2</sup> represents -CH<sub>2</sub>-COOH, -(CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>4</sub>-NH-R<sup>3</sup> wherein R<sup>3</sup> is fluorescein.

11. Process for modifying a nucleic acid fragment comprising enzymatically incorporating at the 3' end of the nucleic acid fragment a modified morpholino-nucleotide having as precursor a compound corresponding to the formula:



in which  $\text{R}^1$  represents a nucleic base,  $m$  is 0 or 1 and  $\text{R}^2$  is selected from the group consisting of:

- $(\text{CH}_2)_n\text{-NH-R}^3$
- $(\text{CH}_2)_n\text{-CO-R}^3$
- $(\text{CH}_2)_n\text{-SR}^3$
- and -  $(\text{CH}_2)_n\text{-OR}^3$

in which  $n$  is an integer ranging from 1 to 12 and  $\text{R}^3$  is selected from the group consisting of photo-crosslinking agents, fatty acids, hydrophobic peptides, antibodies, enzymes, and fluorophores.

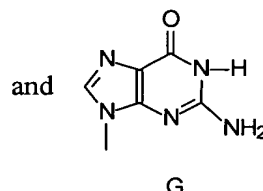
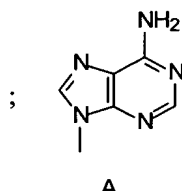
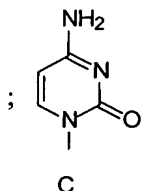
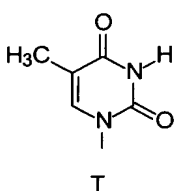
12. Process according to claim 11, in which an enzyme of said enzymatic incorporation is the Klenow fragment of DNA polymerase.

13. Process according to Claim 11, in which an enzyme of said enzymatic incorporation is selected from the group consisting of a heat-resistant polymerase of a *Thermophilus* bacterium, a terminal transferase, and reverse transcriptase.

14. Process according to Claim 11, in which the nucleic base is a natural nucleic base selected from the group

consisting of adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine, and 2-aminopurine.

15. Process according to Claim 11, in which R<sup>1</sup> is selected from the group consisting of:



16. Process according to Claim 11, in which the label is selected from the group consisting of radioactive products, luminescent products, electroluminescent and fluorescent products, and enzymatic labels.

17. Process according to Claim 11, in which R<sup>3</sup> is a fluorophore.

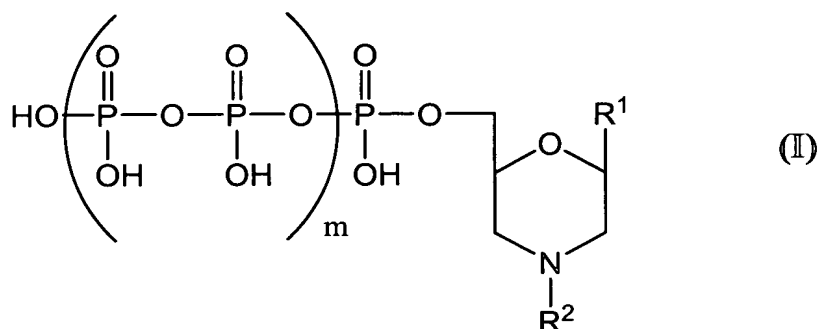
18. Process according to Claim 11, in which R<sup>3</sup> is selected from the group consisting of fluorescein, biotin, and rhodamine.

19. Process according to Claim 11, in which the modified morpholino-nucleotide is compound (I) in which m is 0.

20. Process according to Claim 11, in which R<sup>2</sup> represents -CH<sub>2</sub>-COOH, -(CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>4</sub>-NH-R<sup>3</sup> wherein R<sup>3</sup> is fluorescein.

21. Process for sequencing a nucleic acid comprising the technique of enzymatic polymerization of the sequence

complementary to this nucleic acid using chain terminators at the 3' end of the complementary sequence, in which at least one of the chain terminators has as precursor a compound corresponding to the formula:



in which  $\text{R}^1$  represents a nucleic base,  $m$  is 0 or 1 and  $\text{R}^2$  is selected from the group consisting of:

- |                                   |                                 |
|-----------------------------------|---------------------------------|
| - $(\text{CH}_2)_n\text{-NH}_2$   | - $(\text{CH}_2)_n\text{-SH}$   |
| - $(\text{CH}_2)_n\text{-COOH}$   | - $(\text{CH}_2)_n\text{-OH}$   |
| - $(\text{CH}_2)_n\text{-NH-R}^3$ | - $(\text{CH}_2)_n\text{-SR}^3$ |
| - $(\text{CH}_2)_n\text{-CO-R}^3$ | - $(\text{CH}_2)_n\text{-OR}^3$ |
- and

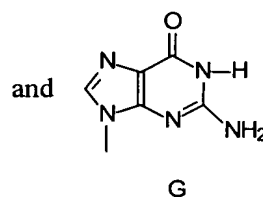
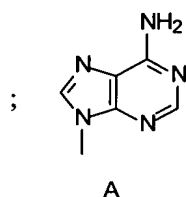
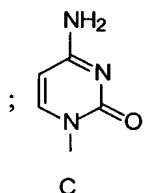
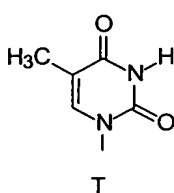
in which  $n$  is an integer ranging from 1 to 12 and  $\text{R}^3$  is selected from the group consisting of a label, a protein, an enzyme, a fatty acid, and a peptide.

22. Process according to Claim 21, in which an enzyme of said technique of enzymatic polymerization is the Klenow fragment of DNA polymerase.

23. Process according to Claim 21, in which an enzyme of said technique of enzymatic polymerization is selected from the group consisting of a heat-resistant polymerase of a *Thermophilus* bacterium, a terminal transferase, and reverse transcriptase.

24. Process according to Claim 21, in which the nucleic base is a natural nucleic base selected from the group consisting of adenine, guanine, cytosine, thymine, uracil, xanthine, hypoxanthine, and 2-aminopurine.

25. Process according to Claim 21, in which R<sup>1</sup> is selected from the group consisting of:



26. Process according to Claim 21, in which the label is selected from the group consisting of radioactive products, luminescent products, electroluminescent and fluorescent products, and enzymatic labels.

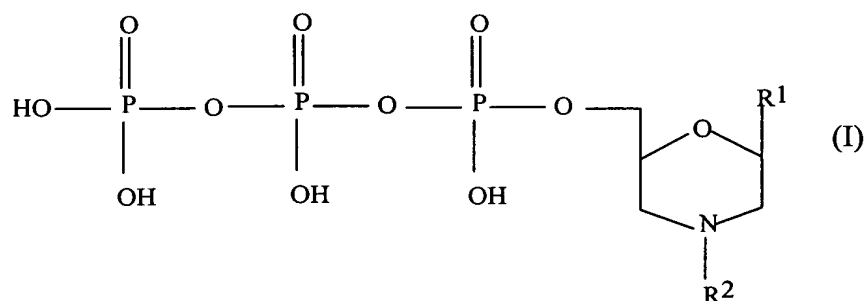
27. Process according to Claim 21, in which R<sup>3</sup> is a fluorophore.

28. Process according to Claim 21, in which R<sup>3</sup> is selected from the group consisting of fluorescein, biotin, and rhodamine.

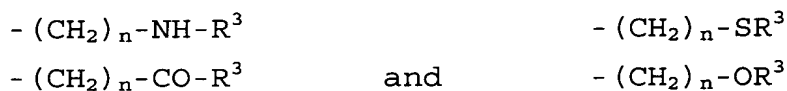
29. Process according to Claim 21, in which said at least one of the chain terminators is compound (I) in which m is 0.

30. Process according to Claim 21, in which R<sup>2</sup> represents -CH<sub>2</sub>-COOH, -(CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub> or -(CH<sub>2</sub>)<sub>4</sub>-NH-R<sup>3</sup> wherein R<sup>3</sup> is fluorescein.

31. Process for manufacturing a morpholino-nucleotide of formula (I):



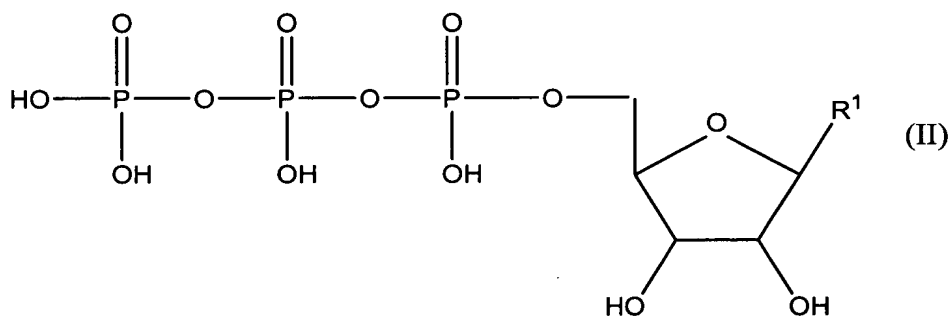
in which R<sup>1</sup> represents a nucleic base and R<sup>2</sup> is selected from the group consisting of:



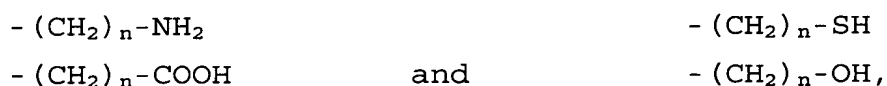
in which n is an integer ranging from 1 to 12 and R<sup>3</sup> is selected from the group consisting of a label, a protein, an enzyme, a fatty acid, and a peptide,

said process comprising

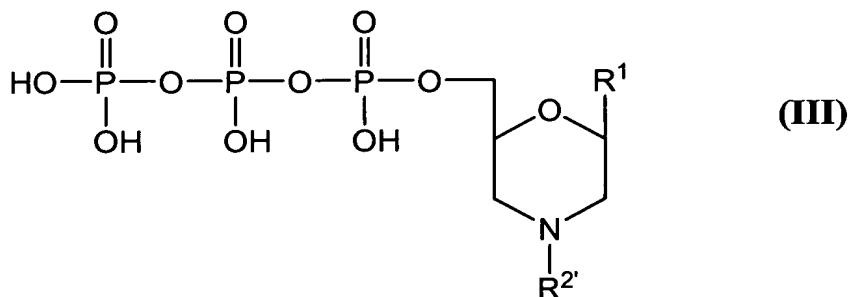
a) reacting a nucleoside triphosphate of formula (II):



with a periodate, a compound of formula R<sup>2'</sup> NH<sub>2</sub>, wherein R<sup>2'</sup> is selected from the group consisting of:



and sodium borohydride to form a morpholino-nucleotide of formula (III):



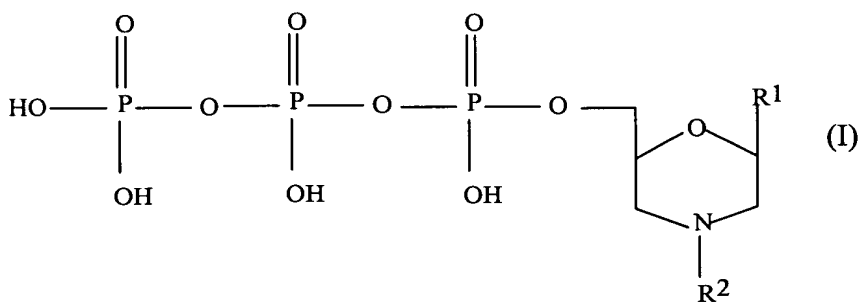
- b) isolating the morpholino-nucleotide of formula (III);  
and  
c) attaching  $R^3$  to the morpholino-nucleotide of formula (III) to form the morpholino-nucleotide of formula (I).

32. Process according to Claim 31, in which  $R^2$  is  $-(CH_2)_n-NH-R^3$  and  $R^3$  is fluorescein.

33. Process according to Claim 32, wherein  $n$  is 4.

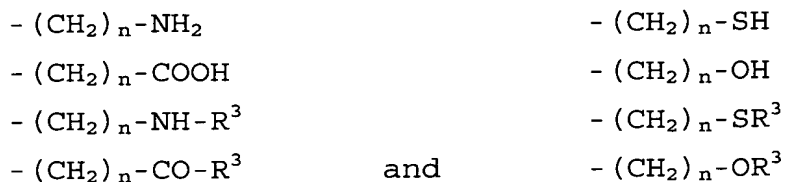
34. Process according to Claim 31, wherein  $R^3$  is a fluorophore.

35. Process for manufacturing a morpholino-nucleotide of formula (I):



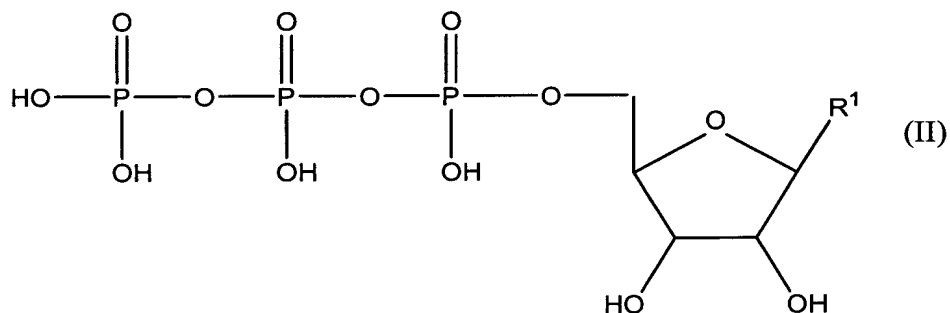
in which  $R^1$  represents a nucleic base and  $R^2$  is selected from the group consisting of:





in which  $n$  is an integer ranging from 1 to 12 and  $\text{R}^3$  is selected from the group consisting of a label, a protein, an enzyme, a fatty acid, and a peptide,

said process comprising reacting a nucleoside triphosphate of formula (II):



with a periodate, a compound of formula  $\text{R}^2\text{NH}_2$ , and sodium borohydride to form the morpholino-nucleotide of formula (I).

36. Process according to Claim 35, wherein  $\text{R}^3$  is a fluorophore.

37. Process according to Claim 35, in which  $\text{R}^2$  is  $-(\text{CH}_2)_n-\text{NH}-\text{R}^3$  and  $\text{R}^3$  is fluorescein.

38. Process according to Claim 37, wherein  $n$  is 4.